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22nd March 1956.

Professor J. Lederberg,
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Dear Josh,

I have not heard anything from you for some time: but I suspect this may be my fault.

Several bits of news. The first is that I have just had an invite from Demerec to L.S.H. for Symposium, and to work there for summer; I can't leave here for more than a month or so, so don't know if they will want me on those terms, but I hope so. I feel quite startled at their generosity in inviting people, fares paid, who don't even have to give a paper.

For various reasons I am anxious to get the abortive transduction paper in before then: and I have therefore taken up the tedious task of finishing off MS. I will enclose current draft with this (or send it separately, as 2nd Class Air Mail, to save postage). I intend to try and prune a bit further, and also to be perhaps a bit less dogmatic, in particular to revise the section comparing your results and mine. Could you glance through it and see I have said nothing too terrible? I am sorry I cannot include photos of pedigree figures, but you have had sketches of these before so I hope will be able to follow O.K., and the same in the case of diagrams to illustrate hypotheses.

When you have looked through, could you let me know what you intend to do about publishing your own paper? I think I will send mine to the J. gen. Microbiol; in your last letter I think you spoke of sending yours to something more genetical, which seems a good idea. If you can let me know I can make the necessary amendments as to "the accompanying paper" etc. (I have begun to put in refs. to it as "L.1956" which I suppose will be O.K. wherever you send it).

You asked for more detailed comments on your draft.

I will reserve ^ethose for end of this letter.

When you go through draft, could you please look out for any places I may have inadvertently misquoted you? (or not mentioned that I got some method from you?) In the discussion you will see I have made use of your ideas to clarify my own; but on the assumption that your paper will soon be available I have not discussed some of the more general hypotheses which you consider.

One or two bits of relevant research news. Chris Quadling and I have done an experiment which we think rules out Bisset's theory on distribution of all parental flagella to one daughter cell in Salmonella etc. The experiment is a very simple one. He grew up L.T.2 in broth at 37°, mean no. of flagella per cell c 8, and made about the same. Then transfer to 45°: growth continues at same rate as before, but mean no. of flagella per cell falls to new steady value of about 0.1 (it varies a bit). During the change (which begins 1-2 generations after transfer) the mode moves down from 6 to 1 (or zero, if you include this class), and there is never the bi-modal distribution with peaks at 6 and 0 predicted by Bisset's theory. We shall try it on B. at J.G.M. Symposium in April. (I think I must send him news of it, as he is apt to explode with slightest stimulus). This makes me much happier about identification of mcp with flagellum (or basal granule). Chris also has fairly good evidence of correlation of distribution of numbers of ^{muta}progeny, in experiments in which synthesis of mcp in a peculiar S. para C is halted by temperature shift (37° → 20°, surprisingly enough). I think when he has finished there will be little doubt about this identification.

Madame Margerie (formerly Hottinguer) and I have been working away on the 'segregation' of serological type in SW 666 treated with i lysates: the character scored is time to cessation of translational movement in H serum (x 100 titre); this is more or less log normally distributed, I am using the mode to summarise. "Initials" are immob. in 5-10" by either serum. Cells with one mcp are immobilised more slowly, even if both donor and recipient are b (? diminished chance of entanglement) Cells which have had one mcp transmitted through many generations ^{are} even, we first thought, not immobilised at all by anti-serum; but it now looks as though they are, but with a modal time of over one generation time: of course this might be result of distal and of flagellum (only) having i reactivity, from earlier generations.

In the course of these experiments we have done ~~three~~ ^{some} pedigrees: one E cell at 12th. generation, and the general picture, convince me that situation is as in SW 541 with the following

del. in manuscript, with dist. of no. of
"yellow" in stained prep. - x

differences: (1) Fewer E cells (usually). (2) Most E cells cease to be so within a few generations, (3) much smaller probability of "accidental immobilisation" (4) (probably) fewer mcp produced per generation. The only thing which you report and I have not seen is "slowing-down" of cell with one mcp a bit before, it is "lost".

In the same experiments we have come on a peculiar situation which you may have seen too. Viz., the M clones behave very erratically as to proportion of M cells in sub-clones. Experiments so far in one clone are compatible with loss and regain, by "mutation", of ability to make mcp at rates of c 10^{-2} per cell per generation, but in another clone under examination at the moment results so far are a mess. All of 3 or 4 clones met with since we began to look for it have behaved in the same general way. (For all I know it may be universal in ordinary motile strains, and so account for, for instance, the usual non-motile minority, and non-Poisson^{ly} large class of cells with zero-flagella). It may be relevant to 'flares' and certainly explains some earlier odd results in clones.

I have been asked to do a monograph in same series as Beale's, on transduction and transformation. I would not mind having a go at it if I could arrange the time. Do you know if anyone in U.S. is on similar project? I would like your opinion on whether I should take this on.

I hear from various rumours that you are going to Melbourne: I hope this works out, if it is what you want to do (but I hope you manage to take in London en route).

Your Paper.

Content. The experimental side seems fine, so far as I can judge without the tables and pedigrees. I feel in a way its a pity you never (so far as I know) tried SW 541 pedigrees, since I feel sure that, with present knowledge, you would at once have got pedigrees which you would consider capable of disproving my hypothesis if its wrong; I think we are agreed that results in your paper neither establish nor disprove it. Apart from this negative one, I have no general criticism.

Theoretical. I admire your logical presentation of all possible alternatives (it has helped me a lot). The hypothesis that mcp = chromonemetal fragments seems less plausible when as now appears, mcp are generated in situations where transduction is not concerned (e.g. SW 553)

Your "Suggestion 5". Should you not specify that gene products do or not 'dilute-out', and if so, if final level of one per cell permits synthesis?

Terminology. I still prefer 'unilinear transmission' to catenate, etc. and shall I think stick to it. I see no particular reason why we should use a single set of words if our preferences differ. (I have used 'original' cell for what you call an 'initial'. I may change this). Otherwise no comment.

Presentation. I suspect that a reader unfamiliar with the material might have considerable trouble in following your paper: but the inclusion of tables, pedigrees and figures will help, and the tidying-up which no doubt has been done since the draft I saw. Anyway its hard for me to judge, the test would be to try it on someone who has never heard of it before.

This seems to cover all I have to say at the moment.
Hope to hear from you soon.

Yours.

Bruce

B.Stocker.

Burnet is over here at the moment, so I shall pump him about your and Esther's plans: if you do take in S.K. in your itinerary, I ~~would~~ ^{am} willing to give a few lectures on the like, let me know, & I will pass the word to the right people. Everyone would v. much like to see & hear you in person.

Love to Esther: & thanks for notes (I could not follow all the bits, but I hope my became too involved)

Re my draft. Still missing are Summary: and a short section at end of experimental part on "results with other strains" (SW544, SL160 (= SW666), and SW578). I guess you can imagine these bits.

Any chance that you will be at CSH, or within reach, in June?